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Remarks

§112 ¶2 Rejection

Claims 2, 3, 20-27, 30, 32, 33, 35 and 36 were rejected under 35 U.S.C. 112 ¶2 as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants respectfully traverse. The Examiner believes that claim 2 recites "wherein said dispersing agent comprises from about 20 to about 70 percent by weight of said dispersing agent," and that it is confusing since the comparison of percentages is with the same agent rather than the weight of the agent compared to the total weight of the dosage form. Applicants respectfully note that claim 2 has no such language but that claim 3 does have similar language. However, claim 3 has additional language which should satisfy the Examiner's concern. Claim 3 reads "A flash-melt pharmaceutical dosage form according to claim 2 wherein said dispersing agent comprises from about 20 to about 70 percent by weight of said dispersing agent *based on the total weight of said dosage form.*" (emphasis added). Applicants believe that this language, which was present in the claims as filed, reflects the clarity the Examiner is seeking. Similarly, the remaining claims rejected under this section of the statute also have this clarifying language. Therefore, Applicants respectfully request the §112 ¶2 rejection to be withdrawn.

§103(a) Rejection

Claims 1-48 were rejected under "35 U.S.C. 103(a) as being unpatentable over WO 98/03064 to Sullivan." Applicants respectfully traverse said rejection. Applicants submit that a detailed examination of Sullivan reveals that it in fact cannot render Applicants' claims *prima facie* obvious.

First, Sullivan is a non-analogous art reference because it is not directed to flashmelt pharmaceutical formulations as is Applicants' invention, but is simply directed to immediate release tablet formulations that are meant to be swallowed. The two are in entirely different classes and the technology suitable for one class would not suggest to anyone skilled in the art that it would be useful in the other. A thorough reading of Sullivan will reveal that it simply does not teach or suggest that its methods can be used to make a *flashmelt* (orally disintegrating tablets)

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pharmaceutical preparation as do Applicants. Applicants' invention is directed to a pharmaceutical formulation that allows for rapid disintegration of the dosage form on a patient's *tongue*. The only "rapid disintegration" Sullivan discloses is that which occurs in a *beaker*. No where in Sullivan is it taught or suggested that the formulations disclosed therein will rapidly dissolve on the tongue of a patient. Instead, Sullivan's tablets are intended to be swallowed. This is supported by the fact that Sullivan is only able to assert that their formulations will disintegrate when *repeatedly agitated* after being placed in nearly a liter of water heated to 37 °C. (10:16-17) See USP 701 XXII Disintegration Test. Even under these conditions, many of Sullivan's examples take several minutes to disintegrate. Applicants' invention falls in an altogether different class because it allows for rapid disintegration (less than one minute) on the tongue of the patient.

Second, Sullivan is primarily directed to substituting costly superdisintegrants with less expensive "co-disintegrants" in an effort to cut costs in agricultural preparations. Sullivan explains,

[i]t will be understood, however, that in many applications, particularly those used in relatively low unit cost formulations such as in the agricultural field, a *less-than-optimum* disintegration rate may be justified if there is a sufficient cost saving. (2:27-29). (emphasis added)

Thus, Sullivan plainly admits that its method, may result in suboptimal disintegration times which would not be desirable in Applicants' strict pharmaceutical context.

Third, Sullivan cannot render Applicants' invention obvious because it does not teach or suggest the specific amounts of each type of agent and/or excipient Applicants require. For example, despite exemplifying 25% of an active agent (niacinamide), Sullivan expressly admits that the amount of "active agent is *not* critical" and can range "*broadly* from about 10 to 95 wt% of the total composition." (11:5 / 6:1-2) (emphasis added) To the contrary, Applicants claim that the active agent must not be more than about 30% of the total weight of its composition.

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Fourth, Sullivan teaches that calcium silicate may comprise "from about 0.01 to 9.0 wt% preferably about 0.1 to 2.7 wt%." (3:6-7). Applicants claim calcium silicate from 20-70 %wt or more particularly 35-45 %wt which are well outside the ranges Sullivan teaches.

Fifth, Sullivan discloses a superdisintegrant range of about 0.045 to 8.0 wt%, but teaches that much lower ranges of 0.045 to 2.4 wt% are preferred. (3:8). In fact, most of Sullivan's examples use superdisintegrants in amounts of 0.5 % with only one example (where the active agent is dishwashing detergent not a pharmaceutical) showing 3 wt%. (18:20-22). To the contrary, Applicants claim ranges of superdisintegrants of 4 to 8% and more particularly 5 to 7% both being outside Sullivan's preferred range.

Sixth, Sullivan speculates that any number of ingredients can be added to the composition including

lubricants, glidants, *dispersants*, suspending agents, surfactants, and fillers or auxillary binders, which are preferably employed in relatively small amounts, *if any*, i.e., zero up to about 20% by weight of the total solid dosage form more often less than about 10% by weight. However, this amount is *not* critical and may comprise as much as a major proportion by weight . . . (6:23-31) (emphasis added)

Again, this does not suggest let alone teach Applicants' specifically claimed combination of excipients nor Applicants' limitations on the amount of each excipient claimed. Instead, Sullivan merely conjectures about a myriad of excipients that a pharmaceutical development scientist could experiment with.

Seventh, Sullivan mentions "dry granulation" in a laundry-list of suitable tableting methods, but qualifies this in such a manner that one skilled in the art would not be led to believe that this art-preferred low-maintenance tableting method is achievable by the teachings therein. Sullivan states,

[t]he selection of the method depends primarily on the active agent, the ability of the mixture of the disintegrants and active agent to flow freely in the tableting machine or extruder, and

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the cohesiveness of the ingredients. If the active agent can be admixed with the disintegrants to produce a free flowing, dense powder, the mixture can be directly compressed. (4:7-10)

Sullivan does nothing more than pose questions using conditional "if then" statements. It does not teach or suggest that his method will *with any reasonable certainty* allow one skilled in the art to successfully use the preferred method of direct compression and dry granulation. Contrary to Sullivan's lack of teaching in this regard, Applicants explicitly state that "a decided advantage of the formulation of the present invention is that it can be dry-granulated into stable, fine granules that can be directly compressed into pharmaceutically elegant flash-melt oral dosage forms, e.g. tablets, caplets, wafers and the like." (16:1-4)

In respect of the above, Applicants respectfully request that the §103(a) obviousness rejection be withdrawn and the claims be allowed.

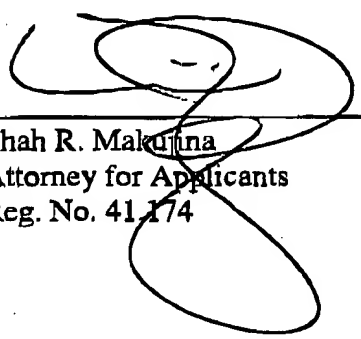
Applicants also wish to draw the Examiner's attention to Form 1449. The record indicates that the Examiner considered some but not all the references noted by Applicants. Specifically, in Applicants' IDS with USPTO stamp of January 17, 2002 under Foreign Patent Documents AK, AM, AN, AO were not considered as they were crossed out and uninitialed. AK refers to EP0890359 and was provided in English. AM, AN and AO are three Japanese patent applications for which English Abstract translations were provided. Applicants request that these references be considered and duly noted as such or in the alternative request clarification. In Applicants' Supplemental IDS with USPTO stamp of June 26, 2002 under Foreign Patent Documents AM, AN, AO, AP and AQ were not considered as they were crossed out and uninitialed. While translations for these Russian applications were not provided, the Russian Search report was provided pursuant to MPEP 609 III. A. A(3). Applicants herein further provide the English abstracts of these Russian patent applications in an attempt to expedite consideration of these references.

Applicants further submit that the claims are in condition for allowance and respectfully request the Examiner's reconsideration.

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